IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: :

    Brophy et al. :

Application No. 10/642,439 :   Art Unit: 1755

Filed: Aug 14, 2003 :   Examiner: James E. McDonough

For: TETHERED CATALYST PROCESSES
IN MICROCHANNEL REACTORS AND
SYSTEMS CONTAINING A TETHERED
CATALYST OR TETHERED CHIRAL
AUXILIARY

                             :   Atty Docket: 02-024

DECLARATION PURSUANT TO 37 CFR § 1.132

1.   I, John H. Brophy, am a co-inventor of the captioned patent application. I earned a PhD in Chemistry from King's College London. I have more than 17 years experience working in the petrochemicals industry in research and development on homogeneous and heterogeneous catalysis processes. I am an author of many papers and patents on catalysis and catalytic processes including the article entitled "Base catalysts immobilised on silica coated reactor walls for use in continuous flow systems," Green Chem. 2004, 6, 193-195.

       The data shows that a tethered catalyst performs significantly better in a flow-by reactor

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configuration as compared to a flow through configuration. The following calculations are based upon our data and the data presented by Haswell et al. in Tetrahedron 60 (2004) 8421-8427. Turnover rate (TOR) is defined as the moles product produced per hour divided by the moles of catalyst.

4.   In our example, 0.9 mmol AMPS was loaded onto each gram of silica wall coating. For an 8 hour run of the Knoevenagel condensation, 1.8×10^{-3} moles reactant (benzaldehyde) per hour were passed through the microchannel having 5.4g of silica wall coating, and 65% of reactant was converted to product for a yield of 1.17×10^{-3} moles product per hour.

So 1.17×10^{-3} moles product was produced per hour over 4.86×10^{-3} mmol catalyst. (1.17 mmol $/ 4.86 \times 10^{-3}$ mmol) equivalent to a TOR = 240.

5.   Haswell et al. conducted the reaction through a packed microchannel containing 5 mg of functionalized silica gel with 4.74×10^{-3} mmols of tethered sites over a 4.75 hour period to yield 0.124 mmol of product (98.9%). TOR = $(0.124 / 4.75) / (4.74 \times 10^{-3}) = 5.5$

6.   Although the tether that we used, 3-aminopropyl (which was derived from 3-aminopropyl-trimethoxysilane (AMPS)) is slightly different than the tether used by Haswell et al., 1-piperazinopropyl; this should not cause a significant change in the reaction rate since both are similar N-based base catalysts. Furthermore, in Table 3, Haswell et al. report similar reactivities for 1-piperazinopropyl-, 3-dimethylaminopropyl, and 3-aminopropyl-functionalized silica. Thus, the observed difference in turnover rate was not a result of slight differences in the type of tethered base catalyst.

7.   Based on my knowledge and experience, there is no reason to believe that the observed improvement, of tethered catalysts in a flow-by configuration versus a flow through

configuration, is limited to the Knoevenagel reaction. I believe that the improvement is generally true. Both myself and Haswell et al. used the Knoevenagel reaction as a model for the general case of using a tethered catalyst in a microchannel reactor.

8.   A chiral auxiliary is not, by itself, a catalyst. A chiral auxiliary is an asymmetric molecule which biases a reaction to favor selective formation of one stereoisomer over another. Chiral auxiliaries are not chiral catalysts. The chiral catalysts described by Hoveyda et al. in US 2004/0019212 are not chiral auxiliaries.

9.   I declare that all of the above statements made of my own knowledge are true and all statements made on information and belief are believed to be true. I understand that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. §1001), and may jeopardize the validity of the application or any patent issuing thereon

Date: 27ᵏʰ MAY 2008   By: _____

                                            John H. Brophy